TechNews

BOOTSTRAPPING BIOLOGY

Sarah Webb explores how DIYbio strategies are helping biologists in traditional labs do better science.

Credit: Erik Jepsen, UC San Diego Publications.

Sophisticated microscopes, DNA sequencers, and a range of prepared kits and reagents have become mainstays of the modern life science laboratory. These tools allow researchers to carry out complicated experiments quickly and conveniently. But the development of such easy-to-use aides comes with some downsides. In addition to purchase and maintenance costs, specialized instruments and assay kits are often mysterious sealed containers accompanied by an instruction manual. Users don't truly understand how they are assembled or how they work, which can cause problems when things go wrong.

"When something doesn't work, or there is something unexpected, you cannot figure out what is going on because you are working with things that you don't master," says Gianpaolo Rando, a biotechnologist who is the chief technology officer and co-founder of a startup company called SwissDeCode.

As high-end laboratory tools become more sophisticated, a wave of DIYbio or biohacking initiatives and communities have sprung up around the globe to support biology research outside the traditional halls of academia and industry. Biohackers come from many corners of society: artists and designers interested in exploring scientific tools, hobbyist scientists, students, educators, and professional researchers who are looking for a creative outlet outside of their primary job.

Such communities typically operate on slim budgets, using donated, modified, or even hand-built equipment. Though these challenges might look like constraints, biohacking—and the skills that come from being forced to think outside the black box of expensive tools—often leads to interesting science.

Right environment, right time

Five years ago, Rando's science career looked very traditional: He had completed a PhD in pharmacology in Milan, Italy and a postdoc in nutrigenomics in Lausanne, Switzerland, before taking an academic position in Geneva. But in 2013, a food scandal rocked in Europe—a subset of hamburger products sold in supermarkets were found to contain horse DNA. Soon afterward, while working on his postdoctoral project, Rando discovered a simple, robust strategy for DNA testing that didn't require strict temperature control.

An easy test, like this one, he thought, could be a tool for quickly checking the DNA of meat and other foods being sold. In 2014, he learned about a local biohacking space, Hackuarium, and saw an opportunity to develop this idea in an environment where he wouldn't be pushed by academic competition and the pressure to publish. In 2016, he left the university, and he is now working for his startup company full-time.

Spaces such as Hackuarium in Lausanne or BioCurious in Santa Clara, California, provide unique blends of workspace, equipment, community, and access to expertise. The first application of Rando's DNA testing idea, BeerDeCoded, was a crowdfunded project that has collected genomic data from various beers, with the goal of creating a beer "family tree." Such information could be useful for beer drinkers interested in discovering new brews and also as a quality-control measure for homebrewers and microbreweries.

"There's very little done on the microbiome and the genetics of beer microbes, and at the same time you know it's something you can easily have a conversation about. So we merged these two interests and launched this project," says Luc Henry, a co-founder of Hackuarium who has also worked on BeerDeCoded.

Lucia Prieto-Godino, a postdoc at the University of Lausanne, has used 3-D printing and other DIYbio tools to build and modify instruments for studying *Drosophila* neurogenetics. Credit: Ana Silbering.

The team found ways to use simple, low-cost equipment, including Bento Lab—a prototype device developed in the United Kingdom that includes a small version of a centrifuge, thermocycler, and gel electrophoresis apparatus within a laptop-sized gadget priced less than \$1250 (for pre-order). But acquiring reagents and supplies can be both expensive and challenging, Rando soon learned. When they needed silica gel for DNA purification, for example, he looked for a way to modify easily available items. In this case, he ended up pulverizing silica-based cat litter.

Working in an environment that mixed professional scientists and the science-curious brought other benefits too, according to Rando. Because he was developing a test that he wanted anyone to be able to use, he asked non-scientists to trial early versions.

“I wanted to simplify the kit. I wanted to make it more user-friendly,” he notes. Just seeing how a designer handled his test kit, he realized that he needed to remove a step that involved using a pipette.

Though hacker spaces are spawning commercial ventures, these communities thrive on open source hardware and software, and the sharing culture that goes along with them. One recent success story from BioCurious is OpenPCR, a project that started out as an open source kit for building a low-cost thermocycler. The original kit was \$500, notes Maria Chavez a board member of BioCurious. The team eventually developed a fully assembled Open qPCR

instrument starting at less than \$3800, roughly an order of magnitude lower than the typical \$30,000 price tag. “There are a lot of mid-level researchers that don’t have the equipment they need, and there are a lot of researchers, especially out of the country, that can’t afford US prices for buying the latest life tech equipment,” she adds.

Developing world, developing tools

Bridging some of those technology gaps in Africa helped Lucia Prieto-Godino bring a hacking mind-set back to her own research on *Drosophila* neurogenetics. While studying for her PhD at the University of Cambridge, she took an intensive course at the Marine Biological Laboratory in Woods Hole, Massachusetts, where she met Sadiq Yusuf, a Nigerian scientist working in Uganda at the time. She knew that few African researchers had the chance to do similar work in *Drosophila* and wondered if she could help with training. After completing her PhD in 2011, she contacted Yusuf to see if there was some way that she could teach students in Africa. Several other researchers signed on as well, and the effort snowballed into an NGO called Teaching and Research in Natural Sciences for Development in Africa, also known as TreNDinAfrica.

But one challenge of teaching and carrying out research in the developing world is having the right tools. Even with donations, Prieto-Godino says, “we were always improvising equipment because we never had exactly what we needed.” A donated fluorescence microscope might lack a camera, so they would add a cheap webcam and support it with chopsticks and tape. As time went on, the team formalized some of their open hardware tools, strategies that used Arduinos—electrical microcontrollers with a simple open source programming language—and Raspberry Pis—small, inexpensive programmable computers. They plan to incorporate these tools within a future Open Biology course in Africa. (André Maia Chagas of the University of Tübingen in Germany has led much of the open source hardware work, Prieto-Godino says, including the development of an open source instrument for studying *Drosophila* known as FlyPi.)

That ability to improvise continues to influence her research as she sets up her own independent laboratory at the Francis Crick Institute in the United Kingdom. Prieto-Godino tinkered with electronics as a PhD student to assemble LEDs for behavioral studies in *Drosophila*, so when she needed a custom behavioral and optogenetics assembly for her postdoctoral research, she felt prepared for the task. She also rigged up an electrophysiology assembly that would record as she stimulated the fly.

Ordering a commercial system would have been expensive and time consuming. Her institution’s workshop

Biohacking has provided new options for less expensive hardware. This Open qPCR instrument by Chai BioTechnologies of Santa Clara, CA, starts at less than \$3800. Credit: www.chaibio.com.

could have helped build something to her specifications, but they were busy, and she knew she could assemble what she needed faster and more easily with the help of her laboratory's 3-D printer. People in many labs have done this type of work, she notes, but her experiences in Africa gave her the knowledge and confidence to do the online research and set it up herself. "The ability to quickly modify your equipment to do exactly what you want to do, that's what's very powerful."

DIY and documentation

Sometimes pursuing an interesting idea means building the tools by any means necessary. Tobey Wenzel, now a postdoc in chemical engineering and biotechnology at the University of Cambridge, is a physicist who has always been interested in biointegration. As a PhD student, he looked for a way to integrate cyanobacteria within solar cells to generate electricity. The problem was that the project was his own idea, and his adviser didn't have grant funding or the relevant instrumentation. "I couldn't buy a lot of expensive equipment. So I started building a lot of things from scratch," he says.

The ability to control, customize, and automate your own system is powerful and can often lead to better tools than something purchased off the shelf, according to Wenzel. But that DIY process also showed him some of the inherent challenges in sharing, replicating and improving hardware built using 3-D printing, Raspberry Pis, Arduinos, and other open source or inexpensive parts. Documentation is a huge bottleneck, and he's been thinking about strategies that will help researchers document exactly what they built and how they built it.

Without this support structure, it can be hard for other researchers to build off these initial designs and refine or improve them. In addition, he notes, even if a PhD student or postdoc builds custom equipment, it might not get much use after that person leaves that laboratory, in part because other members of the group don't know the details of how the instrument was built and how to maintain it.

Wenzel developed DocuBricks, an XML text editor that prompts a user to fill in key information about a DIY hardware project in a standard way. Researchers can also make the project modular, he notes. A DocuBricks file for a DIY microscope might include positioning, optics, and illumination components. But when broken down into individual modules, another user can take advantage of a single piece, such as the positioning module, for another hardware project.

Like some researchers involved with DIYbio, Wenzel is part of the Global Open Source Hardware (GOSH) movement, a group that had their first meeting at CERN in 2016. At that time, the GOSH community decided that they needed a formalized way to communicate and publish open hardware projects. Those discussions ultimately led to the *Journal of Open Hardware*, which launched at the second GOSH meeting in March 2017 in Santiago, Chile. Wenzel, a chief proponent of the project, is an Editor-in-Chief.

Biohacking comes full circle

Some academic institutions are beginning to latch on to the biohacker ethos in ways that take research back to its bootstrapping roots. Many academic researchers still equate high-quality research with expensive, top-of-the-line facilities and equipment. But DIYbio enthusiasts such as Wenzel push against that stereotype.

"I don't want it to be seen as the cheap alternative that's kind of low-quality," says Wenzel. For his part, Henry thinks that there's plenty of room for academic scientists to think about situations when they might not need super-sophisticated equipment and expensive reagents. It's one thing to be concerned and cautious about contaminating a unique and invaluable human tissue sample, he says, but the same level of reagents and tools might not be needed in more routine experiments, such as parallelizing hundreds of minipreps from bacteria.

Biohacking communities can also provide scientists with an influx of enthusiasm and a chance to chew on interesting ideas that might not be marketable projects at work. Biochemist Eric Espinosa, who works for a San Francisco Bay Area biotech startup, has been inspired by some of the interesting basic research ideas

that pop up at BioCurious, such as building vaccines in algae, and is helping to move them forward. It's also a place where some students have an easier time getting started in science: some of BioCurious's members are students who can't find the right research opportunity in the competitive climate of the Bay Area, Chavez says. Hackarium also has a number of student members, who are either working with other scientists or are looking for a lab space to carry out projects in the evenings, after university labs are closed.

Biohacking is also inspiring how the University of California San Diego trains some of its PhD students.

Biohacking tools and resources

Looking for a way to infuse DIYbio into your lab? The DIY BIO website (<https://diybio.org>) provides a roadmap to communities, issues, projects, discussions, and resources. A wealth of inexpensive tools and resources are available for building and modifying biological equipment. Raspberry Pi (www.raspberrypi.org) is a small computer the size of a credit card, that can be programmed for a range of applications. Arduino (www.arduino.cc) is an open-source platform for assembling electronics. Various microcontrollers are available that can be operated with a user-friendly programming language.

Other biohackers might have engineered a solution that you could use or modify further. Examples include the OpenPCR kit (<http://openpcr.org/>) and Open qPCR instrument (www.chaibio.com/openqpcr), the Bento lab (www.bento.bio), and FlyPi (<https://open-labware.net/projects/flypi/>).

A lot of open hardware information resides online in various wikis, but there is a move toward journal-type publications. Resources include the *Journal of Open Hardware* (<https://openhardware.metajnl.com/>), Elsevier's *HardwareX* (www.journals.elsevier.com/hardwarex), and O'Reilly's BioCoder newsletter (www.oreilly.com/biocoder).—S.W.

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Biophysicist Philbert Tsai of UCSD has directed a Hacker Lab course sequence for a small group of quantitative biology PhD students since 2015. Credit: Erik Jepsen, UC San Diego Publications.

The interdisciplinary quantitative biology (qBio) specialization incorporates a Hacker Lab into its course sequence. Now in its third year, the Hacker Lab gives selected students in bioengineering, biological sciences, chemistry, biomedical sciences, and physics access to tools such as 3-D printers, laser cutters, and a CNC milling machines. Students learn basic electronics, Arduino programming, and MATLAB coding for controlling software, microfluidic fabrication, and optical microscopy. During the initial bootcamp, they build some instruments from scratch, such as a wide-field or laser-scanning microscope, says biophysicist Philbert Tsai, who has taught the course since 2015. The end goal isn't for the students to routinely build whole instruments but rather for them to understand modern instrumentation well enough that they could adapt it. Over the next two quarters, they work in interdisciplinary teams looking at interesting biological questions and building tools and equipment to answer them. "[The course is] a combination of programming, image analysis, data acquisition, motor control, fabrication all geared towards building stuff for biological science investigation," Tsai adds.

In the day-to-day grind of research, it's all too easy to let instrumentation guide the work. "Well, what equipment do I have, and what experiments can I do with it?" Tsai says. The hacker approach encourages students to look for the interesting scientific mysteries and then troubleshoot what equipment or modifications they'd need to investigate those questions. Mature scientists often pick up these skills over the course of their careers, he notes, but this type of training allows researchers to hone that expertise and mine that creativity much earlier. The program has also sparked some new bottom-up collaborations between research groups, inspired by graduate students from different disciplines with the expertise to make it possible.

In many ways, the ethos of DIYbio is science coming full circle. Rando notes that much of his appreciation for the back-to-basics mind-set came from his mentor at the University of Geneva, who would roam the laboratory each morning, asking researchers about the experiments and their results, with pointed questions about reagents and concentrations and an eye for careful reverse engineering instead of rigidly following the manufacturer's instructions. Breaking out of the instruction manual mind-set can be as simple as looking through old textbooks or reading patent applications for commercial products, he says. That old-school approach to reagents and instrumentation isn't biohacking, but it's an attitude that Rando worries some researchers are losing.

Written by Sarah Webb, Ph.D.

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